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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,116	01/16/2001	Vedrana S. Susulic	0630/1E791-US1	3094

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EXAMINER
LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
1636	10

DATE MAILED: 07/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/761,116	Applicant(s) SUSULIC ET AL.	
	Examiner Gerald Leffers	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 22-37* is/are pending in the application.

4a) Of the above claim(s) *1,2 and 22-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,29,31-33 and 35-37* is/are rejected.

7)☒ Claim(s) *30 and 34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group IV (claims 28-37) in Paper No. 9, mailed 4/26/02, is acknowledged.

Cancellation of claims 3-21 in papers filed on 1/16/01 is acknowledged. Claims 1-2, 22-37 are pending in this application, with claims 1-2 and 22-27 withdrawn from consideration as being directed towards nonelected inventions.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28, 31-33 and 35-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each of the rejected claims is drawn towards a method of screening for a compound that inhibits activity of a Beta3 adrenergic receptor (B3-AR) *trans*-activating factor by contacting human cells capable of producing the B3-AR factor with a test compound and detecting modulation of the *trans*-activating factor. The specification defines a B3-AR *trans*-activating factor as including "binding factors that may interact with genomic DNA sequences present on the approximately 7 kb DNA upstream of the B_3-AR start site" (page 10, lines 21-22). A critical

element of the claimed invention is the combination of *trans*-activating factor and cognate binding sequence within the 7 kb region upstream of the B3-AR coding sequence. Thus, the rejected claims therefore encompass a potentially large number of different *trans*-activating factors/binding sites that are involved in B3-AR expression in human cells.

The only such factors described at all in the specification are SP-1 and the factor that binds to segment B of the enhancer element described in the instant specification. No other such binding factor/binding site is described in the specification. In fact, no *trans*-activating factor is identified for segment C of the enhancer element described in the instant specification. There is no description in the instant specification of a structural/functional characteristic for one of skill in the art to envision other combinations of *trans*-activating factor/cognate binding sites that are encompassed by the rejected claims.

The prior art does not describe other transcriptional factors/sites involved in the expression of B3-AR in human cells. Therefore, the prior art does not offset the deficiencies of the instant specification regarding description of enough combinations of *trans*-activating factor and cognate binding site to describe the entire genus of such factors encompassed by the rejected claims.

Given the broad genus of *trans*-activating factors/binding sites encompassed by the rejected claims and the lack of any basis provided by the prior art and instant specification for one of skill in the art to envision embodiments other than the embodiments described in the instant specification, one of skill in the art would not be able to envision a sufficient number of *trans*-activating factors involved in expression of B3-AR to describe the genus of such factors

embraced by the claims. Therefore, one of skill in the art would conclude that applicants were not in possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 is vague and indefinite in that the metes and bounds of the term "express at very low level, B3-AR" are unclear. How much of B3-AR can be expressed by the cell for it to remain at a "very low level". This concept does not appear to be defined clearly in the specification and should be deleted from the claim language.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 28-29, 31 are rejected under 35 U.S.C. 102(a) as being anticipated by Ito et al.

Ito et al teach the characterization of B3-AR gene regulatory elements in transgenic mice in which the native B3-AR gene has been knocked out (e.g. Abstract). B3-AR regulatory elements from both the mouse and human genome were characterized. The human B3-AR was

expressed only in brown adipose tissue (BAT), while the mouse B3-AR was expressed in both BAT and white adipose tissue (WAT). Smaller constructs comprising the B3-AR regulatory elements (e.g. -0.6 kb and -14.5 kb) expressed the B3 adrenergic receptor in the same pattern as the largest 74 kb construct. The B3-AR agonist CGP-12177 stimulated oxygen consumption in mice expressing human but not mouse B3-AR. The addition of the agonist CGP-12177 necessarily constitutes contacting cells capable of producing B3-AR *trans*-activating factor with a test compound. The observation that the agonist resulted in an increase in oxygen consumption is evidence that the activity of B3-AR was increased and that at least one B3-AR *trans*-activating factor was involved.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28, 33, 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Granneman et al (U.S. Patent 5,364,772; see the entire patent).

The Granneman patent teaches the construction of vectors comprising the upstream regulatory elements of the rat B3-AR gene operatively linked to a reporter gene (e.g. Examples 7-8) and host cells comprising the reporter gene (e.g. Example 9). The host cells can be those that express fat-specific transcription factors or demonstrate the ability to differentiate into an adipocyte phenotype in vitro (e.g. Example 9). The host cells can be used to test compounds for their ability to modulate expression of B3-AR (e.g. Example 10). An increase or decrease in reporter gene activity in such experiments necessarily reflects an effect on activity of factors that bind the rat B3-AR regulatory region. The Granneman patent also characterizes the coding sequences for the human B3-AR receptor. Granneman et al teach that the B3 receptor is widely considered to be a target for agents that will be useful as human therapeutics (e.g. column 1, lines 19-25).

The Granneman patent does not explicitly teach the use of constructs bearing the human B3-AR regulatory elements in their methods of screening for modulatory compounds.

It would have been obvious to construct vectors comprising the upstream elements for the human B3-AR gene for use in the screening methods taught by Granneman et al because the Granneman patent teaches it is within the skill of the art to utilize such upstream regulatory elements to screen for compounds that affect the expression of the B3-AR protein. One would have been motivated to do so in order to identify compounds that affect the expression of the human B3-AR protein, which Granneman et al teach is widely considered to be a target for

agents useful as human therapeutics. Absent any evidence to the contrary, there would have been a reasonable expectation of success in utilizing the methods taught by the Granneman patent to clone the upstream regulatory elements of the human B3-AR gene and use them to identify agents that modulate B3-AR expression.

Conclusion

Claims 28-29, 31-33, 35-37 are rejected. Claims 30 and 34 are objected to as being dependent on rejected claims. Claims 30 and 34 would be allowed, however, if rewritten in independent form comprising each of the limitations of the claims upon which they are currently dependent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

ggl
July 15, 2002

DAVID GUZO
PRIMARY EXAMINER